

August 1, 1956

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Dear Jerry,

Thank you for your long and interesting letter which was forwarded to me here. First, about polyglycine II. The calculations are at Cambridge. I will send them to you when I get back. From memory they appear similar to yours. However they are not very relevant as we think it unlikely that polyglycine II is as simple as all that. For example, there is no reason why all the chains should run in the same direction. In fact we think it probable that in all synthetic polymers the chains are likely to run at random in both directions and if reversing a chain doesn't make much difference to the way it packs with its neighbours, then one gets a good X-ray pattern. If it upsets the pack, then the X-ray pattern is poor. Notice that reversing a DNA duplex makes no difference at all--this may explain why the X-ray photos are so extremely good; probably better than any other fibre. Two of the rings in polyglycine II (2.47A and 2.11A) are diffuse, so we expect this is due to some effect of this sort. Had you done any calculations along these lines?

I don't think one can apply to fibres the sort of criteria which one applies to single crystals. In this case it seems clear to me that the broad agreement in spacings and intensities shows that a structure of the general type we have described is certainly correct. The unit cell is obviously very small, and

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there are hardly any other ways in which one could build models. It is easy to show that if the unit cell is trigonal (or pseudo-trigonal), so that the polypeptide chain has a three-fold screw, there are only two possible ways of building the backbone. To find the correct arrangement, however, from a powder photograph is not going to be easy. However we shall be taking up the calculations again when I get back to Cambridge and I will let you know how they turn out.

Remel
About virus structure. I enclose the reprints. I find it difficult to understand how 432 would fit Caspar's results (if you read his argument carefully) though naturally the virus could be 23, pseudo 532. However you will be glad to hear that Caspar did optical transforms of a good number of different point patterns, and also that Aaron Klug has solved the general problem of the transforms of 23, 432, and 532, using spherical harmonics and half-order Bessel functions. Incidentally, the source for 532 was F. H. C. C., but none the worse for that. Michael (Crick) has made us a large number of the regular and semi-regular solids, including the stellated ones, using Cundy and Rollet as a crib.

Our most interesting news concerns the "synthetic RNA" (Ochoa type) polymers. I expect by now you will have seen the note by Alex and David in J. A. C. S. about poly A + poly U, which I think explains itself. Meanwhile Jim has taken better X-ray pictures of poly A, which suggest that the unit cell is bigger than we thought, having an equatorial spacing at about $15\frac{1}{2}$ Å. We have therefore built a two-chain model of poly A, using the pairing shown you in Fig. 1. In addition, we have made a hydrogen bond from the other H of the NH_2 to the phosphate of the opposite backbone. This pulls the phosphate inwards and tilts the base in the process, thus explaining why the 3.8 spacing is not 3.4 Å. We have calculated the transform and the agreement is very good, including spacings (discovered by Jim), at 1.9 Å and 1.7 Å. The only doubt is the very low orders, which will be changed by the Na^+ and H_2O , for which so far we have made no allowance, but we hope to do this shortly. We also do not know the shape of the base of the unit cell, since there is nothing between the $15\frac{1}{2}$ Å spacing and the $15\frac{1}{2}/2$ spacing on the equator.

All this leads us to think that poly AU (ie. a random copolymer of A and U), which has an X-ray photo just like RNA,

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may be two parallel intertwined chains, with occasional A-A pairing as we believe it occurs in poly A. When the bases don't pair we assume that the phosphate of the backbone will be at a greater radius. This would explain the strong low order reflection in poly AU. Thus we have, to our embarrassment, arrived at a structure not too unlike the one dreamt up by you and Gunther.

We should very much like some further details about this structure, as Gunther was vague. The tricks appear to be

1. allowing guanine to go to another tautomeric form. I can't say I like this. This would also allow it to pair with adenine. This would be no use for a replicating structure, but is O. K. for a "mating" structure, which is what Gunther wants. Incidentally a number of people, including myself, are doubtful of the biological necessity of a mating structure for RNA.
2. turning over two of the bases. But which two? Gunther couldn't remember. I'd be surprised if you could turn over the pyrimidines without getting bad van der Waal contacts. Adenine can be turned over; in fact this is what is implied in the parallel-chain model of poly U + poly A (the A backbone is reversed compared to DNA), but the NH_2 of guanine has to be watched. I would very much appreciate a brief account of where the model really is, and naturally the coordinates if you have them, even if they are only rough. *what*

induced The only other relevant local news is that Sid Bernhard (and Peter Geiduschek) believe that the base pairs in DNA may show indirect dipole effects i.e. the bases, when paired, may be in the form in which electrons have shifted to give strong electrostatic interactions. This may explain some of the titration anomalies. I also suspect that the G + C pairing could be improved, but I'm not exactly sure how. I think our pairing is bad because its difficult to put anything else (i.e. H_2O) onto that NH position of guanine.

I shall be back in England by about August 9th. Alex and Jane are going to Woods Hole early in August. If you do find time to

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write perhaps you could send a copy to Alex. Do give my best wishes to Pat. Odile and the little girls have been staying with her Mother in Norfolk, and appear to be very fit and cheerful. Alex sends his best wishes and says he hopes he'll be in Washington next time you visit.

~~Sincerely yours,~~ *Yours ever*

F. H. C. Crick, Ph.D.